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**TRANSMITTAL
FORM**

(to be used for all correspondence after initial filing)

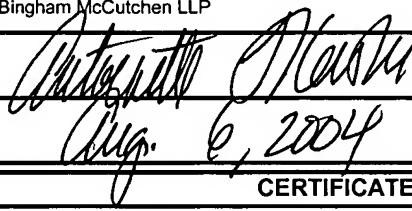
		Application Number	10/681,418
		Filing Date	October 7, 2003
		First Named Inventor	H. Michael SHEPARD
		Art Unit	1623
		Examiner Name	Lawrence E. Crane
Total Number of Pages in This Submission	31	Attorney Docket Number	NB 2008.01

ENCLOSURES (check all that apply)

<input checked="" type="checkbox"/> Fee Transmittal Form	<input type="checkbox"/> Drawing(s)	<input type="checkbox"/> After Allowance Communication to Group
<input type="checkbox"/> Fee Attached	<input type="checkbox"/> Licensing-related Papers	<input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences
<input type="checkbox"/> Amendment / Reply	<input type="checkbox"/> Petition	<input type="checkbox"/> Appeal Communication to Group (Appeal Notice, Brief, Reply Brief)
<input type="checkbox"/> After Final	<input type="checkbox"/> Petition to Convert to a Provisional Application	<input type="checkbox"/> Proprietary Information
<input type="checkbox"/> Affidavits/declaration(s)	<input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address	<input type="checkbox"/> Status Letter
<input type="checkbox"/> Extension of Time Request	<input type="checkbox"/> Terminal Disclaimer	<input checked="" type="checkbox"/> Other Enclosure(s) (please identify below):
<input type="checkbox"/> Express Abandonment Request	<input type="checkbox"/> Request for Refund	115 Reference, postcard receipt
<input checked="" type="checkbox"/> Information Disclosure Statement	<input type="checkbox"/> CD, Number of CD(s) _____	
<input type="checkbox"/> Certified Copy of Priority Document(s)		
<input type="checkbox"/> Response to Missing Parts/ Incomplete Application		
<input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53		

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or individual name	Antoinette F. Konski Bingham McCutchen LLP	
Signature		
Date	Aug. 6, 2004	

CERTIFICATE OF MAILING

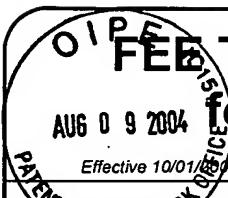
I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below.

Typed or printed name	May R. Zimmerman	Date	Aug. 6, 2004
Signature			

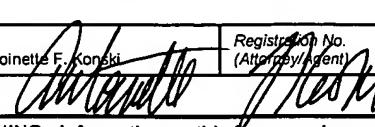
This collection of information is required by 37 CFR 1.15. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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 FEE TRANSMITTAL for FY 2004 AUG 09 2004		Complete if Known	
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		Filing Date	October 7, 2003
		First Named Inventor	H. Michael SHEPARD
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TOTAL AMOUNT OF PAYMENT (\$) <input type="text" value="180"/>		Attorney Docket No.	
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METHOD OF PAYMENT (check all that apply)		FEE CALCULATION (continued)																																																																																																																																																											
<input type="checkbox"/> Check <input type="checkbox"/> Credit card <input type="checkbox"/> Money <input type="checkbox"/> Other <input type="checkbox"/> None <input checked="" type="checkbox"/> Deposit Account: Deposit Account Number: <input type="text" value="50-2518"/> Deposit Account Name: <input type="text" value="Bingham McClellan LLP"/>		3. ADDITIONAL FEES <table border="1"> <thead> <tr> <th>Large Entity</th> <th>Small Entity</th> </tr> </thead> <tbody> <tr> <td>Fee Code</td> <td>Fee (\$)</td> <td>Fee Code</td> <td>Fee (\$)</td> </tr> <tr> <td>1051</td> <td>130</td> <td>2051</td> <td>65</td> <td>Surcharge - late filing fee or oath</td> </tr> <tr> <td>1052</td> <td>50</td> <td>2052</td> <td>25</td> <td>Surcharge - late provisional filing fee or cover sheet.</td> </tr> <tr> <td>1053</td> <td>130</td> <td>1053</td> <td>130</td> <td>Non-English specification</td> </tr> <tr> <td>1812</td> <td>2,520</td> <td>1812</td> <td>2,520</td> <td>For filing a request for reexamination</td> </tr> <tr> <td>1804</td> <td>920*</td> <td>1804</td> <td>920*</td> <td>Requesting publication of SIR prior to Examiner action</td> </tr> <tr> <td>1805</td> <td>1,840*</td> <td>1805</td> <td>1,840*</td> <td>Requesting publication of SIR after Examiner action</td> </tr> <tr> <td>1251</td> <td>110</td> <td>2251</td> <td>55</td> <td>Extension for reply within first month</td> </tr> <tr> <td>1252</td> <td>420</td> <td>2252</td> <td>210</td> <td>Extension for reply within second month</td> </tr> <tr> <td>1253</td> <td>950</td> <td>2253</td> <td>475</td> <td>Extension for reply within third month</td> </tr> <tr> <td>1254</td> <td>1,480</td> <td>2254</td> <td>740</td> <td>Extension for reply within fourth month</td> </tr> <tr> <td>1255</td> <td>2,010</td> <td>2255</td> <td>1,005</td> <td>Extension for reply within fifth month</td> </tr> <tr> <td>1401</td> <td>330</td> <td>2401</td> <td>165</td> <td>Notice of Appeal</td> </tr> <tr> <td>1402</td> <td>330</td> <td>2402</td> <td>165</td> <td>Filing a brief in support of an appeal</td> </tr> <tr> <td>1403</td> <td>290</td> <td>2403</td> <td>145</td> <td>Request for oral hearing</td> </tr> <tr> <td>1451</td> <td>1,510</td> <td>1451</td> <td>1,510</td> <td>Petition to institute a public use proceeding</td> </tr> <tr> <td>1452</td> <td>110</td> <td>2452</td> <td>55</td> <td>Petition to revive - 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late filing fee or oath	1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet.	1053	130	1053	130	Non-English specification	1812	2,520	1812	2,520	For filing a request for reexamination	1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	1251	110	2251	55	Extension for reply within first month	1252	420	2252	210	Extension for reply within second month	1253	950	2253	475	Extension for reply within third month	1254	1,480	2254	740	Extension for reply within fourth month	1255	2,010	2255	1,005	Extension for reply within fifth month	1401	330	2401	165	Notice of Appeal	1402	330	2402	165	Filing a brief in support of an appeal	1403	290	2403	145	Request for oral hearing	1451	1,510	1451	1,510	Petition to institute a public use proceeding	1452	110	2452	55	Petition to revive - unavoidable	1453	1,330	2453	665	Petition to revive - unintentional	1501	1,330	2501	665	Utility issue fee (or reissue)	1502	480	2502	240	Design issue fee	1503	640	2503	320	Plant issue fee	1460	130	1460	130	Petitions to the Commissioner	1807	50	1807	50	Processing fee under 37 CFR 1.17 (q)	1806	180	1806	180	Submission of Information Disclosure Stmt	8021	40	8021	40	Recording each patent assignment per property (times number of properties)	1809	770	2809	385	Filing a submission after final rejection (37 CFR § 1.129(a))	1810	770	2810	385	For each additional invention to be examined (37 CFR § 1.129(b))	1801	770	2801	385	Request for Continued Examination (RCE)	1802	900	1802	900	Request for expedited examination of a design application	Other fee (specify) _____				*Reduced by Basic Filing Fee Paid		SUBTOTAL (3) (\$ 180)	
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SUBMITTED BY		Complete (if applicable)	
Name (Print/Type)	<input type="text" value="Antoinette F. Konski"/>	Registration No. (Attorney/Agent)	<input type="text" value="34,202"/>
Signature			Telephone <input type="text" value="609-849-4950"/>
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PTO/SB/08A (08-03)

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U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Substitute for form 1449A-PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet

1

of

7

Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623

Attorney Docket Number

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U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number – Kind Code ² (if known)			
1	US-3,852,266		12-03-74	Kiyanagi et al.	
2	US-4,247,544		01-27-81	Bergstrom, et al.	
3	US-4,267,171		04-12-81	Bergstrom, et al.	
4	US-4,542,210		09-17-85	Sakata et al.	
5	US-4,668,777		05-26-87	Caruthers et al.	
6	US-4,816,570		03-28-89	Farquhar	
7	US-4,948,882		08-14-90	Ruth	
8	US-4,963,263		10-16-90	Kauver	
9	US-4,963,533		10-16-90	De Clercq et al.	
10	US-4975,278		12-04-90	Senter et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YY	Name of Patentee or Application of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ – Number ⁴ – Kind Code ⁵ (if known)				
11	DE 32 29 169 A1		02-09-84	De Clercq et al.		
12	EP 0 311 107 A2		04-12-89	Stichting REGA VZW		
13	EP 0 311 108A2		04-12-89	Stichting REGA VZW		
14	EP 0 316 592		05-24-89	Stichting REGA VZW		
15	GB 982 776		02-10-65	The Wellcome Foundation		
16	RO 88451		01-30-86	Antibiotics Enterprise, Iasi		X
17	WO 89/05817		06-29-89	Nucleic Acid Research Institute		
18	WO 90/03978		04-19-90	Stichting REGA VZW		
19	WO 91/17424		11-14-91	Vical, Inc.		

Examiner's Signature

Date Considered

* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

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20	US-5,070,082		12-03-91	Murdock, et al. (I)	
21	US-5,077,282		12-31-91	Murdock, et al. (II)	
22	US-5,077,283		12-31-91	Murdock, et al. (III)	
23	US-5,085,983		02-04-92	Scanlon	
24	US-5,116,822		05-26-92	De Clercq et al.	
25	US-5,116,827		05-26-92	Murdock, et al. (IV)	
26	US-5,133,866		07-28-92	Kauver	
27	US-5,137,724		08-11-92	Balzarini et al.	
28	US-5,212,161		05-18-93	Morinire et al.	
29	US-5,212,291		05-18-93	Murdock, et al. (V)	

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		Country Code ³ – Number ⁴ – Kind Code ⁵ (if known)				
30	WO 92/19767		11-12-92	Terrapin Technologies, Inc.		
31	WO 93/06120		04-01-93	University of Rochester		
32	WO 94/03467		02-17-94	Institute of Organic Chemistry & Biochemistry of the Academy of Sciences of the Czech Republic, et al.		
33	WO 94/22483		10-13-94	Kozak, Alexander		

Examiner's Signature	Date Considered
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* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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34	US-5,217,869		06-08-93	Kauver	
35	US-5,233,031		08-03-92	Borch et al.	
36	US-5,264,618		11-23-93	Felgner et al.	
37	US-5,300,425		04-05-94	Kauver	
38	US-5,338,659		08-16-94	Kauver, et al.	
39	US-5,430,148		07-04-95	Webber, et al.	
40	US-5,433,955		07-18-95	Bredehorst et al.	
41	US-5,457,187		10-10-95	Gmeiner et al.	
42	US-5,459,127		10-17-85	Felgner et al.	
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		Country Code ³ – Number ⁴ – Kind Code ⁵ (if known)				
44	WO 95/01806		01-19-95	Kondratyev, A.		
45	WO 95/08556		03-30-95	Amersham International, Inc.		
46	WO 95/09865		04-13-95	Terrapin Technologies, Inc.		
47	WO 95/12678		05-11-95	Connors, T. et al.		
48	WO 96/03151		02-08-96	Springer et al.		
49	WO 96/07413		04-04-96	University of Georgia Research Foundation & Yale University		

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Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
Attorney Docket Number	NB 2008.01

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50	US-5,521,161		05-28-96	Malley et al.	
51	US-5,527,900		06-18-96	Balzarini et al.	
52	US-5,596,018		01-21-97	Baba et al.	
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54	US-5,627,165		05-06-97	Glazier	
55	US-5,645,988		07-08-97	Vande Woude et al.	
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60	WO 96/10030		04-04-96	Isis Pharmaceuticals, Inc.		
61	WO 96/23506		08-08-96	Fraunhofer Society for the Promotion of Applied Research E.V.		X
62	WO 96/29336		09-26-96	Medical Research Council, University College Cardiff Consultants, Inc. Rega Foundation		

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63	US-5,981,507		11-09-99	Josephson et al.	
64	US-6,057,305		05-02-00	Holý et al.	
65	US-6,245,750		06-12-01	Shepard	
66	US-6,339,151		02-15-02	Shepard et al.	
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71	WO 96/33168		10-24-96	Kumai Chemical Industry Co Ltd et al.		
72	WO 96/40088		12-19-96	Hostetler, Karl Y.		
73	WO 96/40708		12-19-96	La Jolla Pharmaceuticals, Inc.		
74	WO 96/40739		12-19-96	Terrapin Technologies, Inc.		
75	WO 97/25342		07-17-97	Terrapin Technologies, Inc.		
76	WO 97/28179		08-07-97	Fick, James & Israel, Mark		

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77	WO 97/49717		12-31-97	Balzarini et al.		
78	WO 98/49177		11-05-98	University College Cardiff Consultants Limited		
79	WO 99/06072		02-11-99	Boehringer Mannheim Corp.		
80	WO 99/08110		02-18-99	NewBiotics, Inc.		
81	WO 99/20741		04-29-99	Geron Corporation		
82	WO 99/23104		05-14-99	The Government of the United States of America represented by The Secretary of Health & Human Services		
83	WO 99/37753		07-29-99	NewBiotics, Inc.		

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				Application Number	10/681,418
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				First Named Inventor	H. Michael SHEPARD
				Art Unit	Lawrence E. Crane
				Examiner Name	1623
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		WO 00/18755	04-06-00	University College Cardiff Consultants Limited and Rega Foundation	
	84	WO 00/33888	06-15-00	Dubois, V. et al.	
	85	WO 01/07088	02-01-01	NewBiotics, Inc.	
	86	WO 01/83501	11-08-01	University College Cardiff Consultants Limited and Rega Foundation	
	87	WO 01/85749	11-15-01	University College Cardiff Consultants Limited and Rega Foundation	
	88				

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Art Unit	Lawrence E. Crane
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	1	ABRAHAM et al. "Synthesis and biological activity of aromatic amino acid phosphoramidates of 5-fluoro-2'-deoxyuridine and 1-β-arabinofuranosylcytosine: Evidence of phosphoramidase activity" <i>J. Med. Chem.</i> (1996) 39:4569-4575	
	2	AKDAS et al. "Glutathione S-transferase and multidrug-resistant phenotype in transitional cell carcinoma of the bladder" <i>Eur. Urol.</i> (1996) 29(4):483-486	
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	4	ALMASAN et al. "Genetic instability as a consequence of inappropriate entry into and progression through S-phase" <i>Cancer Metast. Rev.</i> (1995) 14:59-73	
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	10	BAGSHAWE, K.D. "Antibody-directed enzyme prodrug therapy: A review", <i>Drug Develop. Res.</i> (1995) 34(2):220-230	
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	14	BALZARINI et al. "Mechanism of anti-HIV action of masked alaninyl d4T-MP derivatives" <i>PNAS USA</i> (July 1996) 93 :7295-7299	
	15	BANERJEE et al. "Molecular mechanisms of resistance to antifolates, a review" <i>Acta Biochim. Pol.</i> (1995) 42 (4):457-464	
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	17	BARBATO et al. "Synthesis of bridged pyrimidine nucleosides and triazo [4, 3-c] pyrimidine nucleoside analogues" <i>Nucleos. Nucleot.</i> (1989) 8 (4):515-528	
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	29	CARRERAS and SANTI "The catalytic mechanism and structure of thymidylate synthase" <i>Annu. Rev. Biochem.</i> (1995) 64 :721-762	
	30	CARTER et al. "Humanization of an anti-p185 ^{HER2} antibody for human cancer therapy" <i>PNAS USA</i> (May 1992) 89 :4285-4289	

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Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623

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	45	DeCLERCQ et al. "Antiviral Activity of Novel Deoxyuridine Derivatives" <i>Current Chemotherapy: Proceedings of the International Congress of Chemotherapy</i> published in <i>Virology</i> (Sept. 18, 1978) 1:352-354	
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	58	FELMINGHAM and WASHINGTON "Trends in the antimicrobial susceptibility of bacterial respiratory tract pathogens – findings of the Alexander Project 1992-1996" <i>J. Chemotherapy</i> (1999) 11(Suppl 1):5-21	
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				Art Unit	Lawrence E. Crane
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	72	HSAIO and BARDOS "Synthesis of 5'-thymidinyl bis(1-aziridinyl)phosphinates as antineoplastic agents" <i>J. Med. Chem.</i> (19810 24 :887-889		T ²
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	78	JONES and MANN "New methods of synthesis of β -aminoethylpyrazoles" <i>J. Am. Cancer Soc.</i> (Aug. 20, 1953) 75 :4048-4052		
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	85	LEE et al. "Inhibition of mouse thymidylate synthase promoter activity by the wild-type p53 tumor suppressor protein" <i>Exp. Cell Res.</i> (1997) 234:270-276	
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	100	McINTEE "Probing the mechanism of action and decomposition of amino acid phosphomonoester amides of antiviral nucleoside prodrugs" <i>J. Med. Chem.</i> (1997) 40 :3323-3331	
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Sheet 10 of 19

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Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
Attorney Docket Number	NB 2008.01

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				Filing Date	October 7, 2003
				First Named Inventor	H. Michael SHEPARD
				Art Unit	Lawrence E. Crane
				Examiner Name	1623
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Sheet 12 of 19

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First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
Attorney Docket Number	NB 2008.01

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Sheet

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Complete if Known

Application Number	10/681,418
Filing Date	October 7, 2003
First Named Inventor	H. Michael SHEPARD
Art Unit	Lawrence E. Crane
Examiner Name	1623
Attorney Docket Number	NB 2008.01

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher city and/or country where published	T ²
	201	GROS et al. "Isolation and expression of a complementary DNA that confers multidrug resistance" <i>Nature</i> (Oct. 1986) 323:728-731	
	202	GROS et al. "Mammalian multidrug resistance gene: Complete cDNA sequence indicates strong homology to bacterial transport proteins" <i>Cell</i> (Nov. 7, 1986) 47:371-380	
	203	GROS et al. "Isolation and characterization of DNA sequences amplified in multidrug-resistant hamster cells" <i>PNAS USA</i> (Jan. 1986) 83:337-341	
	204	GUDKOV et al. "Cloning and characterization of DNA sequences amplified in multidrug-resistant djungarian hamster and mouse cells" <i>Somat. Cell Mol. Genet.</i> (1987) 13(6):609-619	
	205	HAKIMELAHI et al. "Design, synthesis and structure-activity relationship of novel dinucleotide analogs as agents against herpes and human immunodeficiency viruses" <i>J. Med. Chem.</i> (Nov. 10, 1995) 38(23):4648-4659	
	206	HARDY et al. "Atomic structure of thymidylate synthase: Target for rational drug design" <i>Science</i> (Jan. 23, 1987) 235:448-455	
	207	HARRIS et al. "Adenovirus-mediated p53 gene transfer inhibits growth of human tumor cells expressing mutant p53 protein" <i>Cancer Gene Ther.</i> (1996) 3(2):121-130	
	208	HASHIMOTO et al. "Simple separation of tritiated water and [³ H]deoxyuridine from [5- ³ H]deoxyuridine 5'-monophosphate in the thymidylate synthase assay" <i>Anal. Biochem.</i> (1987) 167:340-346	
	209	HENGSTSCHLÄGER et al. "The role of p16 in the E2F-dependent thymidine kinase regulation" <i>Oncogene</i> (1996) 12:1635-1643	
	210	HOLÝ et al. "Structure-Antiviral Activity Relationship in the Series of Pyrimidine and Purine N-[2-(2-Phosphonomethoxy)ethyl] Nucleotide Analogues. 1. Derivatives Substituted at the Carbon Atoms of the Base" <i>J. Med. Chem.</i> (1999) 42(12):2064-2086	
	211	HORIKOSHI et al. "Quantitation of thymidylate synthase, dihydrofolate reductase, and DT-diaphorase gene expression in human tumors using the polymerase chain reaction" <i>Cancer Res.</i> (Jan. 1, 1992) 52:108-116	
	212	HORN et al. "Fialuridine is phosphorylated and inhibits DNA synthesis in isolated rat hepatic mitochondria" <i>Antivir. Res.</i> (1997) 34:71-74	
	213	HUANG and SANTI "Active site general catalysts are not necessary for some proton transfer reactions of thymidylate synthase" <i>Biochemistry</i> (1997) 36:1869-1873	
	214	HUDZIAK et al. "Selection for transformation and met protooncogene amplification in NIH 3T3 fibroblasts using tumor necrosis factor α " <i>Cell Growth & Differentiation</i> (1990) 1:129-134	

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				Art Unit	Lawrence E. Crane
				Examiner Name	1623
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	215	HUSAK et al. "Pseudotumour of the tongue caused by herpes simplex virus type 2 in an HIV-1 infected immunosuppressed patient" <i>Brit. J. Dermatol.</i> (1998) 139:118-121		T ²
	216	IMAI et al. "Studies on phosphorylation. IV. Selective phosphorylation of the primary hydroxyl group in nucleosides" <i>J. Org. Chem.</i> (June 1969) 34(6):1547-1550		
	217	JOHNSTON et al. "Production and characterization of monoclonal antibodies that localize human thymidylate synthase in the cytoplasm of human cells and tissue" <i>Cancer Res.</i> (Dec. 15, 1991) 51:6668-6676		
	218	JOHNSTON "The role of thymidylate synthase expression in prognosis and outcome of adjuvant chemotherapy in patients with rectal cancer" <i>J. Clin. Oncol.</i> (Dec. 1994) 12(12):2640-2647		
	219	KAMB "Cyclin-dependent kinase inhibitors and human cancer" <i>Curr. Top. Microbiol. Immunol.</i> (1998) 227:139-148		
	220	KATKI et al. "Prodrugs activated by thymidylate synthase: Treatment of tumors with deoxyuridine analogs" <i>Proc. Amer. Assoc. Cancer Res.</i> (March 1998) 39:Abstract No. 1275		
	221	KLECKER et al. "Toxicity, metabolism, DNA incorporation with lack of repair, and lactate production for 1-(2'-fluoro-2'-deoxy-β-D-arabinofuranosyl)-5-iodouracil in U-937 and MOLT-4 cells" <i>Mol. Pharmacol.</i> (1994) 46:1204-1209		
	222	KNIGHTON et al. "Structure of and kinetic channelling in bifunctional dihydrofolate reductase-thymidylate synthase" <i>Nature Struct. Biol.</i> (March 1994) 1(3):186-194		
	223	KODAMA et al. "Evaluation of antiherpetic compounds using a gastric cancer cell line: Pronounced activity of BVDU against herpes simplex virus replication" <i>Microbiol. Immunol.</i> (1996) 40(5):359-363		
	224	KUMAR et al. "Synthesis and biological evaluation of some cyclic phosphoramidate nucleoside derivatives" <i>J. Med. Chem.</i> (Sept. 1990) 33(9):2368-2374		
	225	KUNDU et al. "Synthesis and biological activities of [E]-5-(2-acetylvinyl) uracils" <i>Eur. J. Med. Chem.</i> (1993) 28:473-479		
	226	KUROBOSHI and HIYAMA "A facile synthesis of difluoromethylene compounds by oxidative fluorodesulfurization of dithioacetals using tetrabutylammonium dihydrogentrifluoride and N-halo compounds" <i>SYNLETT</i> (Dec. 1991) pp. 909-910		
	227	KUROBOSHI and HIYAMA "A facile synthesis of α,α-difluoroalkyl ethers and carbonyl fluoride acetals by oxidative desulfurization-fluorination" <i>SYNLETT</i> (April 1994) pp. 251-252		
	228	LAM "Application of combinatorial library methods in cancer research and drug discovery" <i>Anti-Cancer Drug Design</i> (1997) 12:145-167		
	229	LARSSON et al. "Thymidylate synthase in advanced gastrointestinal and breast cancers" <i>Acta Oncologica</i> (1996) 35(4):469-472		

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First Named Inventor	H. Michael SHEPARD
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	230	LI et al. "Lack of functional retinoblastoma protein mediates increased resistance to antimetabolites in human sarcoma cell lines" <i>PNAS USA</i> (Oct. 1995) 92 :10436-10440	
	231	LIVINGSTONE et al. "Altered cell cycle arrest and gene amplification potential accompany loss of wild-type p53" <i>Cell</i> (Sept. 18, 1992) 70 :923-935	
	232	MASTERS and ALTARDI "The nucleotide sequence of the cDNA coding for the human dihydrofolic acid reductase" <i>Gene</i> (1983) 21 :59-63	
	233	McGUIGAN "Aryl phosphate derivatives of AZT retain activity against HIV1 in cell lines which are resistant to the action of AZT" <i>Antivir. Res.</i> (1992) 17 :311-321	
	234	McGUIGAN "Intracellular delivery of bioactive AZT nucleotides by aryl phosphate derivatives of AZT" <i>J. Med. Chem.</i> (1993) 36 :1048-1052	
	235	McGUIGAN "Aryl phosphoramidate derivatives of d4T have improved anti-HIV efficacy in tissue culture and may act by the generation of a novel intracellular metabolite" <i>J. Med. Chem.</i> (1996) 39 :1748-1753	
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	237	McKAY et al. "Broad spectrum aminoglycoside phosphotransferase type III from <i>Enterococcus</i> : Overexpression, purification, and substrate specificity" <i>Biochemistry</i> (1994) 33 :6936-6944	
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	239	MONTFORT and WEICHSEL "Thymidylate synthase: Structure, inhibition, and strained conformations during catalysis" <i>Pharmacol. Ther.</i> (1997) 76 (1-3):29-43	
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	241	MORRISON & BOYD (eds) <i>Organic Chemistry</i> , Allyn & Bacon, Inc., Boston, MA, (1973) only pages 1170-1180 supplied	
	242	MURAKAMI and SEKIYA "Accumulation of genetic alterations and their significance in each primary human cancer and cell line" <i>Mutat. Res.</i> (1998) 400 (1-2):421-437	
	243	NAESENS et al. "Anti-HIV activity and metabolism of phosphoramidate derivatives of D4T-MP with Variations in the amino acid moiety" Poster Session 1, <i>The Tenth International Conference on Antiviral Research</i> , Hotel Nikko, Atlanta, GA April 6-11, 1997; published in <i>Antivir. Research</i> (April 1997) 34 (2):A54 (Abstract 40)	
	244	NAKANO et al., "Critical role of phenylalanine 34 of human dihydrofolate reductase in substrate and inhibitor binding and in catalysis" <i>Biochemistry</i> (1994) 33 :9945-9952	

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	245	NOOTER and STOTER "Molecular mechanisms of multidrug resistance in cancer chemotherapy" <i>Path. Res. Pract.</i> (1996) 192 :768-780	
	246	OSAKI et al. "5-fluorouracil (5-FU) induced apoptosis in gastric cancer cell lines: Role of the p53 gene" <i>Apoptosis</i> (1997) 2 :221-226	
	247	OSHIRO et al. "Genotoxic properties of (E)-5-(2-bromovinyl)-2'-deoxyuridine (BVDU)" <i>Fundam. Appl. Toxicol.</i> (1992) 18 :491-498	
	248	PARDO et al. "The incorporation of deoxyuridine monophosphate in DNA increases the sister-chromatid exchange yield" <i>Exp Cell Res.</i> (1987) 168 :507-517	
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	250	PERRY et al. "Plastic adaptation toward mutations in proteins: Structural comparison of thymidylate synthases" <i>Proteins</i> (1990) 8 :315-333	
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	253	ROBERTS "An isotopic assay for thymidylate synthetase" <i>Biochemistry</i> (Nov. 1966) 5 (11):3546-3548	
	254	ROGULSKI et al. "Glioma cells transduced with an <i>Escherichia coli</i> CD/HSV-1 TK fusion gene exhibit enhanced metabolic suicide and radiosensitivity" <i>Hum. Gene Ther.</i> (Jan. 1, 1997) 8 :73-85	
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	257	SCHIFFER et al. "Crystal structure of human thymidylate synthase: A structural mechanism for guiding substrates into the active site" <i>Biochemistry</i> (1995) 34 :16279-16287	
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	260	SINGH et al. "Studies on the preparation and isomeric composition of ¹⁸⁶ Re- and ¹⁸⁸ Re-pentavalent rhenium dimercaptosuccinic acid complex" <i>Nucl. Med. Commun.</i> (1993) 14 :197-203	
	261	SLAMON et al. "Human breast cancer: Correlation of relapse and survival with amplification of the HER-2/neu oncogene" <i>Science</i> (Jan. 9, 1987) 235 :177-182	
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	263	SNYDMAN et al. "Analysis of trends in antimicrobial resistance patterns among clinical isolates of <i>Bacteroides fragilis</i> group species from 1990 to 1994" <i>Clin. Infect. Dis.</i> (1996) 23(Suppl. 1):S54-S65	
	264	STASCHKE et al. "The in vitro anti-hepatitis B virus activity of FIAU [1-(2'-deoxy-2'-fluro-1-β-D-arabinofuranosyl-5-iodo)uracil] is selective, reversible, and determined, at least in part, by the host cell" <i>Antiviral Res.</i> (1994) 23:45-61	
	265	STOUT et al. "Structure-based design of inhibitors specific for bacterial thymidylate synthase" <i>Biochemistry</i> (1999) 38:1607-1617	
	266	SUKUMAR and BARBACID "Specific patterns of oncogene activation in transplacentally induced tumors" <i>PNAS USA</i> (Jan. 1990) 87:718-722	
	267	TAKEISHI et al. "Nucleotide sequence of a functional cDNA for human thymidylate synthase" <i>Nucl. Acid Res.</i> (1985) 13(6):2035-2043	
	268	TENNANT et al. "Antiviral activity and toxicity of fialuridine in the woodchuck model of hepatitis B virus infection" <i>Hepatology</i> (July 1998) 28(1):179-191	
	269	TOWNSEND (eds), <i>Chemistry of Nucleosides and Nucleotides</i> , Vol. 3, Plenum Press, New York, NY (1974) only Table of Contents, Bibliography, pages 529-535 and Index pp. 537-552 supplied	
	270	UBEDA and HABENER "The large subunit of the DNA replication complex C (DSEB/RF-C140) cleaved and inactivated by Caspase-3 (CPP32/YAMA) during fas-induced apoptosis" <i>J. Biol. Chem.</i> (Aug. 1, 1997) 272(31):19562-19568	
	271	van de VIJVER et al. "Amplification of the <i>neu</i> (c-erbB-2) oncogene in human mammary tumors is relatively frequent and is often accompanied by amplification of the linked c-erbA oncogene" <i>Mol. Cell. Biol.</i> (May 1987) 7(5):2019-2023	
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	273	WANG et al. "Identification and characterization of Ich-3, a member of the interleukin-1 β converting enzyme (ICE)/Ced-3 family and an upstream regulator of ICE" <i>J. Biol. Chem.</i> (Aug. 23, 1996) 271(34):20580-20587	
	274	YIN et al. "Wild-type p53 restores cell cycle control and inhibits gene amplification in cells with mutant p53 alleles" <i>Cell</i> (Sept. 18, 1992) 70:937-948	
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	276	The American Heritage College Dictionary, Third Edition, Houghton Mifflin Co., New York, NY (1997) only page 668 supplied	

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PATENT
Docket No. NB 2008.01

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application for:

H. Michael SHEPARD et al.

Serial No.: 10/681,418

Filing Date: October 7, 2003

For: ENZYME CATALYZED THERAPEUTIC
COMPOUNDS

Examiner: Lawrence E. Crane

Group Art Unit: 1623

INFORMATION DISCLOSURE STATEMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In accordance with 37 CFR §§ 1.97 and 1.98, the items identified in this Information Disclosure Statement ("IDS") are brought to the attention of the Examiner for consideration in connection with the examination of the above-identified application. The items are listed on the attached forms PTO/SB/08a and PTO/SB/08b.

Copies of the following documents listed in PTO/SB/08a (Item Nos. 1-15, 17-60, 62-65, and 71-88) and copies of the following documents listed in PTO/SB/08b (Item Nos. 1-163) were previously cited by the Office or submitted in Information Disclosure Statements in related applications: U.S. Serial Numbers 09/235,961, filed January 22, 1999, now U.S. Patent No. 6,339,151; U.S. Serial No. 09/856,127, filed July 21, 2000 (U.S. Patent No. 6,683,061 issued January 27, 2004); U.S. Serial No. 09/782,721, filed February 12, 2001; U.S. Serial No. 09/990,799, filed November 16, 2001; and U.S. Serial No. 10/051,320, filed January 18, 2002, and accordingly, copies are not included herewith. The Examiner is requested to make these documents of record.

Pursuant to 37 CFR § 1.98(a)(2)(i), copies of the following items identified on form PTO/SB/08a under the heading U.S. Patent Documents (Item Nos. 66-70) are not attached.

Copies of the following documents listed in PTO/SB/08a (Item Nos. 16 and 61) and PTO/SB/08b (Item Nos. 164-275) are attached for consideration.

The Examiner is requested to make these documents of record.

This Information Disclosure Statement is submitted:

With the new patent application submitted herewith (37 C.F.R. § 1.97(a)).

08/10/2004 SZEWDIE1 00000115 502518 10681418

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- Within three months of the application filing date or before receipt of a first Office Action on the merits; accordingly, no fee or separate requirements are required.
- Before the mailing date of the first Office Action on the merits. In the event, however that an Office Action has crossed in the mail with this Information Disclosure Statement, the Commissioner is hereby authorized to charge Deposit Account No. 50-1189 for any fees required pursuant to 37 C.F.R. §§ 1.17(p) or 1.17(i)(1).
- After receipt of a first Office Action on the merits but before a final Office Action or Notice of Allowance. A fee is required. The Commissioner is hereby authorized to charge Deposit Account No. 50-1189 for any fees required pursuant to 37 C.F.R. §§ 1.17(p) or 1.17(i)(1).
- After receipt of a final Office Action or Notice of Allowance, but before payment of the issue fee. Accordingly, a Certification under 37 C.F.R. § 1.97(e) is provided herein. The Commissioner is hereby authorized to charge Deposit Account No. 50-1189 for any fees required pursuant to 37 C.F.R. §§ 1.17(p) or 1.17(i)(1).

The undersigned certifies that:

- Each item of information contained in the Information Disclosure Statement was first cited in any communication mailed from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this information disclosure statement.
- No item of information contained in this information disclosure statement was cited in a communication mailed from a foreign patent office in a counterpart foreign application or, to the knowledge of the undersigned after making reasonable inquiry, was known to any individual designated in 37 C.F.R. § 1.56(c) more than three months prior to the filing of this Information Disclosure Statement.

Applicants would appreciate the Examiner initialing and returning the Form PTO-1449, indicating that the information has been considered and made of record herein.

This Information Disclosure Statement under 37 C.F.R. § 1.97 is not to be construed as a representation that: (i) a complete search has been made; (ii) additional information material to the examination of this application does not exist; (iii) the information, protocols, results and the like reported by third parties are accurate or enabling; or (iv) the above information constitutes prior art to the subject invention.

In the unlikely event that the transmittal letter is separated from this document and the U.S. Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 50-1178** referencing **7008303001**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: Aug. 6, 2004

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